OFFICE OF NEW ANIMAL DRUG EVALUATION
REVIEWERS' CHAPTER

APPROVAL LETTERS

I. PURPOSE OF GUIDE

This guide is intended to assure uniformity of the approval letter. This guide describes the information that should be included in an approval letter and prescribes the format that should be used by reviewers.

It covers approval letters for original and supplemental New Animal Drug Applications (NADAs), Administrative NADAs, and Abbreviated New Animal Drug Applications (ANADAs). This guide does not describe the Category I supplemental approvals completed by the Division of Manufacturing Technologies (HFV-140). Refer to 21 CFR 5.83(c) for information regarding signature authority for manufacturing supplements and 514.8(a)(4)(iii), (iv), and (v), and (d)(3) for information regarding types of manufacturing supplemental approvals.

II. ELEMENTS OF APPROVAL LETTERS[1]

A. Reference line: The first line of the letter should reference the application by STARS code [NADA or ANADA: original (A), reactivated original (E), supplement (C), or reactivated supplement(R)]. It is not necessary to list codes for amendments.

EX: NADA 141-141 C-0003

[1] The approval letter is intended only to inform a sponsor of the approval and the conditions of approval. It is not intended to provide details to the applicant regarding the basis for CVM's decision to approve. Thus, the approval letter should not specifically discuss findings relevant to particular sections (e.g., environmental, food safety, effectiveness) of an NADA.

The MRA will be the Agency's record of the basis for its decision to approve and the FOI Summary will summarize the basis for approval for the public.

B. Date: The date of the approval letter is added by HFV-107 to the paper copies. The primary divisions add the date of the approval letter to the electronic file using the same date as the paper copy.

C. Address: Address the letter to the company to the attention of whomever signed the cover letter, unless the sponsor otherwise indicates and documentation of such communication is included in the file. The first line should specify the company name, the second line should direct the letter to the attention of a specific individual identified by degrees (if available), the third line should include the position of the individual in the company, the fourth line should include the street address, and the final line should specify the city, state, and zip code. For example:

Drug Company International
Attention: John Doe, DVM, Ph.D.
Manager, Regulatory Affairs
1100 Industrial Drive, suite 500
Anytown, NJ 55555

Use the address provided in the cover letter. This address may not be the same as the corporate address listed in 21 CFR 510.600. The corporate address should be used in the Memorandum Recommending Approval (MRA), Federal Register (FR) notice, and Freedom of Information (FOI) Summary. The address on the envelope should match the inside address of the letter.

D. Salutation: The salutation should respect titles conferred by professional degree, i.e., use Dr. for holders of Ph.D. or veterinary degrees. Use Ms. or Mr. when advanced scientific degrees are not known.

E. Opening paragraph: The first sentence should unambiguously identify the submission by date and submission type and describe the application in terms of the regulatory action requested. The submission should be described by product name (with established name in parentheses). The opening paragraph should also cite any amendments by date and may describe the amendments briefly, if relevant. If there are numerous amendments, they should be listed in a second sentence to keep the first sentence short and focused on the application type and requested regulatory action. If multiple amendments are submitted on the same date, the STARS code, (M-*xxxx*) should be included.

> EX: In an original new animal drug application (NADA) dated January 1, 2000, and amended February 20, 2000, you requested approval of *Tradename <insert trade name in CAPS>* (established name) <*dosage form*> for <*insert the intended uses and conditions of use described in the labeling, including species and/or class*>.

EX: In an original new animal drug application (NADA) dated January 1, 2000, and subsequently amended, you requested approval of *Tradename < insert trade name in CAPS >* (established name) <*dosage form*> for <*insert the intended uses and conditions of use described in the labeling, including species and/or class*>. The original NADA dated January 1, 2000, was amended on <*insert dates of all amendments*>. <*Describe amendments briefly, if relevant*>.

Additional sentences may be necessary to describe relevant regulatory history of the application if the amendments change the conditions of approval originally requested. For example, the removal of a claim (originally requested) from labeling after the data were deemed inadequate by CVM.

EX: Your June 16, 2000, amendment provided revised facsimile labeling which removed claims for persistent efficacy for *C. surnabada*.

F. Second paragraph: The first sentence should read "Your application is approved." The second sentence should inform the sponsor if the approval will be announced by FR notice. This paragraph should also include, as needed, any request for the submission of final printed labeling (FPL), including any minor changes[2] that are requested by CVM to be made to labeling, prior to marketing.

EX: Your application is approved. A notice of this approval is being forwarded for publication in the FEDERAL REGISTER. Prior to distribution and marketing, three copies of each component of the final printed labeling must (21 CFR §514.1(b)(3)(vi)) be submitted to CVM. This labeling should be identical to the facsimile labeling submitted October 4, 2000 (A0000).

G. Third paragraph: The first sentence should state whether exclusivity was granted or not. If the new animal drug qualifies for exclusivity, include the citation for the section of the Federal Food, Drug, and Cosmetic Act (the Act) that provides for exclusivity (512(c)(2)(F)(i), (ii), (iii), (iv), or (v)) and note the duration. See P&P Guide 1243.5780 for the applicable exclusivity language that should be included in the approval letter. Refer to http://www.fda.gov/cvm/index/policy_proced/1243_5780.pdf .

H. Fourth Paragraph-Manufacturing

Manufacturing paragraph for Original NADAs/ANADAs: This paragraph should discuss the need for process validation and specify the expiration date as provided in the transmittal section from the Division of Manufacturing Technologies (HFV-140) consulting review. The following paragraphs should be used. (NOTE: HFV-140 may provide

[2] Only minor label changes should be listed in an approval letter. Major label changes necessitate an amendment to the underlying application.

additional language to be added to the approval letter if the new animal drug is intended for use in animal feed.)

> EX: Manufacturing process validation is required under GMPs (21 CFR Parts 211 and 226). A product that does not conform to GMPs is adulterated (21 USC 351(a)(1)(B)). If manufacturing process validation information was not available or was found deficient at the time of the pre-approval inspection, the appropriate FDA District Office should be contacted after such validation has been completed on production lots and prior to shipment of the drug product. FDA may take regulatory action if drug products are shipped prior to completion of the validation process.
>
> An expiration dating of *XX* months is acceptable for this product.

Manufacturing paragraph for Administrative NADAs: Here the sponsor should be reminded of their responsibilities for manufacturing process validation and expiration dating. The suggested wording for the paragraph follows:

> Ex. FDA may take regulatory action if any drug products are shipped prior to completion of the validation process. See our letter dated *<cite the technical section complete letter for manufacturing>*. An expiration dating of *XX* months is acceptable for this product.

I. Closing paragraph: This paragraph should include a request that any future correspondence relating to the approval include a citation to this letter by date and NADA/ANADA file number. Note in the approval letter that a request to change the conditions of approval (e.g., manufacturing changes) may require the submission of a supplemental application. See 21 CFR 514.8. Provide the name and telephone number of a CVM contact person(s) from the responsible review Division, i.e., other than the official signing the letter, who will be available to answer questions.

J. Signature: The Center Director signs original applications and significant supplements (new species, significant new claims, changes in prescription / over-the-counter status). The Director, Office of New Animal Drug Evaluation, signs most supplemental applications, except for certain manufacturing supplements.

K. Enclosures: A copy of the Freedom of Information Summary identical to that which will be forwarded to Division of Dockets Management (HFA-305) should be provided to the sponsor with the approval letter. Thus, the enclosure block should note "Enclosure: Freedom of Information Summary."

L. Copies: cc block: The salmon (pink) copy will be filed in the jacket in DCU. Provide copies as follows:

cc:
HFV-199, NADA or ANADA XXX-XXX, X-XXXX, Orig. [salmon copy]
HFV-104, Green Book
HFV-107, Reserve Copy
HFR-*XXxxx*, District Office Copy (original approvals only) [Ex. HFR-SW350, KAN-DO]

<Reviewer name/HFV-#/Date>
<Typist name/HFV-#/Date> [NOTE: typist name used if the reviewer is not the typist].

*Note: Copies of the approval letter should only be sent to the District Offices in which the manufacturing facilities are located. The manufacturing site information will be found in the Chemistry and Manufacturing Controls (HFV-140) technical section complete letter or in the Manufacturing Chemistry review(s). Mailing codes for FDA DOs are provided in P&P Guide 1243.3300, Copies of Correspondence to FDA District Offices.

The sign-off process for the letter should be documented. This means that there needs to be a record of when and who signed the draft and final approval copies of the letter. If the preparer finds it useful, they may use a table to document this information. The table should be placed at the bottom of the letter and should include space for the signing official's mail code, their signature, and the date they signed the draft. See the table below.

Office	Surname	Date Draft Signed	Date Final Signed
Team HFV #			
DD HFV #			
Insert specialty division HFV# (if appropriate)			
QA Team HFV 107			

When the draft has been approved and the preparer is putting the document into final format, the preparer should transcribe the names and dates that the draft copy was signed by typing that information into the table on the final version of the letter. When the final copies are printed and marked for distribution, the table should only appear on the salmon

copy and should not be on the final letter to the sponsor. The final approval signatures and dates on the final approval letter will be written in the table as the document circulates.

If the preparer **does not** use a table, then the preparer should type the draft approval information (i.e., the officials name and the date the draft was signed) on the final printed salmon (a.k.a. HFV-199 copy or pink copy) copy in the cc block. Each person concurring with the final approval action will initial the salmon copy, include their mail code, and the date of signature in the cc block area of the letter.

III. COMMENTS ON STYLE

Preferred references for matters of style are the *Style Manual*, GPO, 1984 and *The Gregg Reference Manual*. Where these references do not address style, such as for scientific notation or new terminology, sources such as the *Council of Biology Editors (CBE) Style Manual* or *American Medical Association Style Manual* are useful.

For addresses, spell out words like "Street", but do not capitalize "suite." The state is identified by its two-letter abbreviation (e.g., MD) both in the address block of the letter and on the envelope. Use two spaces to separate the state abbreviation from the Zip Code on the envelope.

Margins: The top, bottom, and right margins of the approval letter should be 1 inch. The left margin should be 1.25 inches to add a gutter which allows easier reading and photocopying of bound documents.

Headers: A header one inch from the page top identifying the page number and STARS identification number and submission number separated as shown below should be included on the second and subsequent pages.

EX. Page 2- NADA *XXX-XXX* C-*xxxx*

IV. AVAILABILITY OF SAMPLE LETTERS

Attached is an example of an approval letter for an original NADA and granted five years of exclusivity.

V. REFERENCE

Program Policy and Procedures Manual Guide 1243.5780 Exclusivity Wording for Use In the Following Documents: Memorandum Recommending Approval and Letter to Applicant http://www.fda.gov/cvm/index/policy_proced/ppindex.htmlT

VI. SAMPLE LETTER

NADA *XXX-XXX* A-0000

Date of Approval letter is placed here by DCU or HFV-107

Drug Company International
Attention: John Doe, DVM, Ph.D.
Manager, Regulatory Affairs
1100 Industrial Drive, suite 500
Anytown, NJ 55555

Dear Dr. Doe:

In an original new animal drug application (NADA) dated January 1, 2002, and amended January 31, 2002, you requested approval of DRUGEX (drugex hydrochloride) Type A medicated article for increased growth promotion and feed efficiency in broiler chickens.

Your application is approved. A notice of this approval is being forwarded for publication in the FEDERAL REGISTER. Prior to distribution and marketing, three copies of each component of the final printed labeling must be submitted to CVM. This labeling should be identical to the facsimile labeling submitted February 2, 2002 (C0001).

Under section 512(c)(2)(F)(i) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for FIVE years of marketing exclusivity beginning on the date of the approval because no active ingredient of the new animal drug has previously been approved.

Manufacturing process validation is required under GMPs (21 CFR Parts 211 and 226). A product that does not conform to GMPs is adulterated (21 USC 351(a)(1)(B)). If manufacturing process validation information was not available or was found deficient at the time of the pre-approval inspection, the appropriate FDA District Office should be contacted after such validation has been completed on production lots and prior to shipment of the drug product. FDA may take regulatory action if drug products are shipped prior to completion of the validation process.

An expiration dating of 12 months is acceptable for this product.

If you submit any correspondence in the future relating to this approval, you should include a citation to this letter by date and NADA number. Any request to change the conditions of approval may require the submission of a supplemental application. If you have any questions, please contact Dr. White White, Team Leader, Swine and Poultry Drugs Team (301-111-1111).

Sincerely yours,

Title of appropriate signatory

Enclosure: Freedom of Information Summary

cc:
HFV-199, NADA or ANADA XXX-XXX, X-XXXX, Orig. [salmon copy]
HFV-104, Green Book
HFV-107, Reserve Copy
HFR-*XXxxx*, District Office Copy (original approvals only) [Ex. HFR-SW350, KAN-DO]

Office	Surname	Date Draft Signed	Date Final Signed
Team HFV-128		2/1/2002	
DD HFV-120		2/5/2002	
HFV-150		2/7/2002	
QA Team HFV 107		2/10/2002	

MTypist/HFV-128/02/12/2002